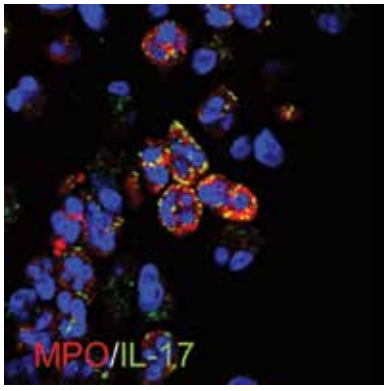
Two-for-One Special

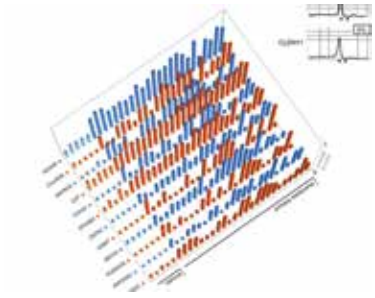
Following 8 months of treatment with the Janus kinase inhibitor tofacitinib citrate, which has been approved for treatment of rheumatoid arthritis, a 25-year-old patient with plaque psoriasis and concomitant alopecia universalis (AU) experienced total regrowth of hair at all body sites, and the remaining psoriasis was no longer bothersome to the patient. Tofacitinib affects T lymphocytes and thus, not surprisingly, mediates inflammatory diseases. Craiglow and King report the first use of effective pathogenesis-based therapy for AU and, more importantly, heralds the positive effects of a single agent for two seemingly disparate diseases with distinct pathomechanisms. ***See page 2988***

The Loop Goes On



The common autoimmune blistering skin disease bullous pemphigoid (BP) involves autoantibody binding; however, additional inflammatory mechanisms are essential for subepidermal blister formation. Le Jan and colleagues demonstrated that, despite the high IL-17 levels in the blister fluids of BP patients, the IL-17-induced inflammatory response was controlled by innate immune cells, including neutrophils but not T helper type 17 cells. A resultant autoamplification loop, which involves upregulation of detrimental proteases by IL-17, may self-reinforce the chronic inflammation and lead to tissue damage in BP patients with severe disease. These findings support additional clinical investigations into modulation of the IL-17 pathway for treatment of bullous autoimmune diseases. ***See page 2908***

Algorithm for Diagnosis



Following a genome-wide methylation screen, Gao and colleagues studied promoter CpG island methylation of selected genes in search of diagnostic markers to facilitate discrimination of melanoma from dysplastic nevi, which is considered an intermediate stage between common nevus and melanoma. Progressive CpG island methylation was revealed, with the lowest levels in common nevi and increasing levels in dysplastic nevi, melanoma, and, finally, metastatic disease. These investigators proposed a diagnostic algorithm to distinguish melanoma from benign lesions. Methylation of *CLDN11*, *CDH11*, *PP1R3C*, and *GNMT* may indicate malignancy, suggesting that examination of these factors may aid in the difficult molecular diagnosis of melanocytic lesions. ***See page 2957***

Halting Progression

In an effort to more carefully define the mechanism of melanoma progression, Lupia and colleagues examined the effects of silencing and overexpression of the tetraspannin CD63 on the epithelial-to-mesenchyme transition (EMT), which is thought to represent the progression of melanoma lesions via changes in invasive, stemness, and metastatic characteristics. Using melanoma cell lines, a mouse xenograft tumor model, and human melanoma biopsies, the investigators demonstrated that CD63 is a potent negative regulator of EMT in melanoma cells, as CD63 silencing resulted in an aggressive phenotype whereas overexpression resulted in reduced cell motility, invasiveness, and tumorigenicity. ***See page 2947***

Bad Hair Days

Hair loss attributable to massive apoptosis of hair matrix keratinocytes is common following chemotherapy; however, no effective treatment to prevent or slow this effect is available, partly owing to our lack of understanding of the underlying mechanism. In an *ex vivo* model of chemotherapy-induced hair loss, Sharova and colleagues demonstrated that early hair follicle response to the widely used anticancer drug doxorubicin involves upregulation of apoptosis-related genes as well as dramatic reorganization of the terminal differentiation programs of the keratinocytes, perhaps paving the way for development of drug-specific hair-protective options for cancer patients. ***See page 2873***

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